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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GAMBEL, PHILLIP	
ART UNIT	PAPER NUMBER
1644	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/051,497	LIN ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,6-13,17,19,20,22-25 and 38* is/are pending in the application.

4a) Of the above claim(s) *7-9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,6,10-13,17,19,20,22-25 and 38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 02/01/2007, has been entered.
Claims 1, 4, 6, 13, 17, 20, 22, 23, 24 and 25 have been amended.
Claim 38 has been added.

Claims 1, 3, 4, 6-13, 17, 19, 20 and 22-25 and 38 are pending.

Claims 2, 5, 14-16, 18, 21, and 26-37 have been canceled previously.

As pointed out previously, applicant's election of species (B), drawn to methods using an anti-PSGL-1 antibody and an agent that binds to the antibody and induces the cross-linking of a plurality of PSGL-1 antigens on the cell surface without traverse in the Reply, filed 07/22/2004, and the species autoimmune disease and type I diabetes in the Reply, filed 03/10/2004, has been acknowledged.

Claims 1, 3, 4, 6, 10-13, 17, 19, 20, 22-25 and 38 are under consideration in the instant application.

Claims 7-9 have been withdrawn from consideration by the examiner 37 CFR 1.142(b), as being drawn to a nonelected invention or species.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Action will be in response to applicant's amendment, filed 02/01/2007.
The rejections of record can be found in the previous Office Action.

Although applicant's amended claims, Declaration and IDSs could lead to a Final Office Action,
this Office Action is made NON-Final in order to address applicant's newly amended claims and arguments / evidence concerning "apoptosis-inducing anti-PSGL-1 antibodies" in the claimed methods in the interest of compact prosecution.

Although certain grounds of rejection are being maintained,
New Grounds of Rejection have been set forth herein to clearly address not only the broadest reasonable interpretation of the claimed methods,
but also to address applicant's arguments and interpretation of the recitation of "apoptosis-inducing anti-PSGL-1 antibodies" in the claimed methods,
again, in the interest of compact prosecution.

3. Priority.

As indicated previously, the filing date of the instant claims is deemed to be the filing date of the instant application USSN 10/051,497, filed 01/18/2002;
as the previous provisional priority application USSN 60/310,196, filed 08/03/2001, does not appear to provide sufficient written description for the claimed "limitations".

Applicant's assertions, filed 02/01/2007, concerning the priority of the instant invention back to priority USSN 60/310,196, filed 8/3/01, are acknowledged.

Applicant's arguments and the examiner's rebuttal are essentially the same of record.

As indicated in the previous Office Action, mailed 07/31/2006,
these assertions have not been found convincing essentially for the reasons of record reiterated herein for applicant's convenience.

As indicated previously, the instant claims now recite limitations which were not clearly disclosed in the priority provisional application as well as the specification as-filed, and would have changed the scope of the priority application and do change the scope of the instant disclosure as-filed.

For example, it cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. See In re Smith 173 USPQ 679, 683 (CCPA 1972) and MPEP 2163.05.

Therefore, applicant's reliance on generic methods to reduce T cell-mediated immune responses with PSGL-1-specific antibodies and certain limitations found in the Examples of the provisional application does not provide sufficient written description for the claimed limitations indicated previously and herein, as currently claimed.

As indicated previously, the filing date of the instant claims as they read on "methods of preventing or reducing a T cell-mediated immune responses in an individual, including the "selecting an individual diagnosed", "administering a compound ... induces a signal transduction pathway that results in the death of the T cell" (e.g. claim 1), "an agent that binds to the monoclonal antibody and induces the cross-linking of a plurality of PSGL-1 antigens on the surface of the T cell" (e.g. claim 4), detecting the number of T cells in a first biological sample (e.g. claims 13-14), "20% of peripheral blood $CD3^+$ cells (e.g. claims 15-16) and "diabetes" (e.g. elected autoimmune disease) is deemed to be the filing date of the instant application USSN 10/051,497, filed 8/3/01, as the previous provisional priority application does not appear to provide sufficient written description for the claimed "limitations" indicated herein.

Here, with respect to the recitation of "detecting the number of T cells in a first biological sample",

applicant relies upon Example 6 of the provisional application USSN 60/310,196, filed 08/03/2001 and likewise Example 6 of the instant application, USSN 10/051,497 to support the description above, via the administration of an anti-PSGL antibody TAB4 to experimental mice, measuring the percentage of $CD3^+$ T cells in harvested spleen and peripheral blood and comparing these results with corresponding results from untreated mice.

Applicant continues to assert that this comparison of control and treated mice is tantamount to what is claimed in claim 13.

However, as pointed out previously, applicant is relying upon a limited experimental study measuring certain parameters under certain defined conditions, while the claims are broader in scope or breadth.

It is acknowledged that page 15, lines 14-20 of the provisional application USSN 60/310,196, filed 08/03/2001, provides written description for targeting "diabetes mellitus" with anti-TAIP compounds (i.e., anti-PSGL-1 compounds)

Although applicant disagrees with this analysis, applicant has not presented a convincing detailed analysis as to why the claimed subject matter has clear support in the parent application, other than to assert that the provisional application provides ample written description for each and every limitation as presented and citing certain passages of the provisional application without sufficiently pointing out written support for the "limitations" indicated previously and herein.

Again, applicant is invited to verify the priority date of the instant claims, including written support and enablement under 35 USC 112, first paragraph.

Again, if applicant disagrees, applicant should present a detailed analysis as to why the claimed subject matter has clear support in the parent application. Applicant is invited to verify the priority date of the instant claims, including written support and enablement under 35 USC 112, first paragraph.

4. With respect to the Information Disclosure Statement, filed 08/07/2006; USSNs 10/662,906, 11/125,837 and 11/127,804 are acknowledged.

However, since applicant did not present these USSNs on the Information Disclosure Statement, they will not be cited on the front page of a U.S. Patent.

5. This is a rejection under 35 USC § 112, first paragraph, "new matter".

Claims 4 and 20 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed.

The specification as originally filed does not provide support for the invention as now claimed:

"an antibody that binds to the monoclonal antibody and induces the cross-linking of a plurality of PSGL-1 antigen on the surface of the T cell".

Applicant's arguments, filed 02/01/2007, have been fully considered but have not been found convincing essentially for the reasons of record.

Applicant's arguments and the examiner's rebuttal are essentially the same of record.

As indicated in the previous Office Action, mailed 07/31/2006,

these assertions have not been found convincing essentially for the reasons of record reiterated herein for applicant's convenience.

Again, it appears that applicant is relying upon the disclosure of the anti-hamster Ig as a cross-linker antibody (e.g. see Example 3 on pages 19-20) to support an entire (sub)genus of "antibodies that bind to the monoclonal antibody and induces the cross-linking of a plurality of PSGL-1 antigen on the surface of the T cell".

In addition, applicant points out that Example 10 discloses another antibody, namely cross-linker rabbit anti-mouse Ig that binds to the monoclonal antibody and induces cross-linking of a plurality of PSGL-1 antigens on the surface of T cells or NK cells.

Therefore, applicant asserts that two (2) examples of cross-linking antibody as claimed have been disclosed.

Applicant also asserts that rather than providing a generic or sub-generic disclosure, applicant provides a disclosure of a particular species of the claimed genus of cross-linking antibodies.

Again, and consistent with applicant's arguments;

applicant's reliance on a generic disclosure (e.g. agent) and limited species (e.g. anti-hamster Ig and rabbit anti-mouse Ig in Examples 3 and 10) does not provide sufficient direction and guidance to the generic "antibody that binds to the monoclonal antibody and induces the cross-linking of a plurality of PSGL-1 antigen on the surface of the T cell", as currently claimed.

It is noted that a generic or a sub-generic disclosure cannot support a species unless the species is specifically described. It cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. See In re Smith 173 USPQ 679, 683 (CCPA 1972) and MPEP 2163.05.

Applicant relies upon the ordinary artisan recognizing the possession of a subgenus of two Examples of cross-linking antibodies based upon certain Examples in the specification as-filed rather than clear written description of the claimed "limitation" in the application as filed and currently claimed.

Applicant has not provided sufficient direction either in the instant application as filed or in the priority application for
"an antibody that binds to the monoclonal antibody and induces the cross-linking of a plurality of PSGL-1 antigen on the surface of the T cell" as currently claimed.

In addition, applicant further submits that it would be appreciated that the claimed genus of cross-linking antibodies includes any suitable anti-isotype antibody, examples of which are so numerous in the prior art.

Obviousness is not the standard for the addition new limitations to the disclosure as filed.
It is noted that entitlement to a filing date does not extend to subject matter, which is not disclosed, but would be obvious over what is expressly disclosed.
See Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1977).

Again, the specification as filed does not provide a sufficient written description nor provide sufficient blaze marks nor direction for the instant methods encompassing the above-mentioned "limitation", as currently recited. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant's arguments have not been found persuasive.

Applicant is required to cancel the new matter in the response to this Office Action.

Alternatively, applicant is invited to provide sufficient written support for the "limitation" indicated above.
See MPEP 714.02 and 2163.06

6. Given, applicant's indication that the claimed methods rely upon secondary cross-linking agents / antibodies to accomplish the claimed mode of action (i.e., apoptosis), whether or not the anti-PSGL-1 antibodies are administered even in the absence of cross-linking agents/antibodies (e.g., see page 13, lines 4-9 of Applicant's Remarks, filed 02/01/2007);

the previous scope of enablement rejection under 35 USC 112, first paragraph, with respect to enabling "anti-hamster Ig" and "rabbit anti-mouse Ig" as "an antibody that bind to the monoclonal antibody and induces the cross-linking of a plurality of PSGL-1 antigens on the surface of cell" has been withdrawn.

Further, the following New Ground of Rejection is based upon the enablement of the claimed methods by the administration of anti-PSGL-1 antigen-binding fragments in the absence of administering secondary cross-linking agents / antibodies.

7. New Ground of Rejection.

Claims 1, 3, 4, 6, 10-13, 17, 19, 20, 22-25 and 38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

In vitro and animal model studies have not correlated well with in vivo clinical trial results in patients. Since the therapeutic indices of immunosuppressive drugs or biopharmaceutical drugs can be species- and model-dependent, it is not clear that reliance on the in vitro and in vivo experimental observations as well as the clinical experience with targeting various inflammatory conditions with PSGL-1 specific antibodies accurately reflects the relative ability or efficacy of the claimed methods *to Induce apoptosis in T cells and NK cells with PSGL-1-specific antigen-binding fragments in the absence of administering secondary cross-linking agents / antibodies.*

Pharmaceutical therapies in the absence of in vivo clinical data are unpredictable for the following reasons; (1) the protein may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the protein; (2) the protein may not reach the target area because, i.e. the protein may not be able to cross the mucosa or the protein may be adsorbed by fluids, cells and tissues where the protein has no effect; and (3) other functional properties, known or unknown, may make the protein unsuitable for in vivo therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment.

See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

Although not all claims recite "antigen-binding fragments" per se,
given that the record is not clear that the claimed "antibodies", including "monoclonal antibodies" read on "antigen-binding fragments" as well,
this rejection as it reads on "antigen binding fragments" is applied to all of the claims at this time.

This invention encompasses administering any "anti-PSGL-1 antigen-binding fragment" to induce apoptosis in T cells and NK cells in the absence of administering cross-linking agents / antibodies.

Applicant's has indicated that the claimed methods rely upon secondary cross-linking agents / antibodies to accomplish the claimed mode of action (i.e., apoptosis), whether or not the anti-PSGL-1 antibodies are administered even in the absence of cross-linking agents/antibodies.
(e.g., see page 13, lines 4-9 of Applicant's Remarks, filed 02/01/2007).

While applicant has acknowledged that Fc binding via Fc receptors may provide an additional mechanism of action that precludes the need for administering secondary cross-linking agents / antibodies,
such a mechanism of action relies upon the administration of anti-PSGL-1 antibodies that have the structural capacity to bind Fc receptors.
Antigen-binding fragments do not necessarily have immunoglobulin Fc components that would enable binding via Fc receptors.

Further, the instant specification as-filed apparently provides limited direction and guidance as to appropriate secondary cross-linking agents / antibodies, namely "anti-hamster Ig" and "rabbit anti-mouse Ig" as "an antibody that bind to the monoclonal antibody and induces the cross-linking of a plurality of PSGL-1 antigens on the surface of cell",

The instant specification as-filed does not appear to provide sufficient enablement for any "antigen-binding fragment of anti-PSGL-1 antibodies" can induce apoptosis of T cells and NK cells in order to reduce cell-mediated immune responses
in the absence of administering secondary cross-linking agents / antibodies.

This invention encompasses any "antibody fragment that binds to the monoclonal antibody and induces the cross-linking of a plurality of PSGL-1 antigens on the surface of cell" (e.g. see Summary of the Invention, particularly page 5, paragraph 3 of the instant specification), yet the instant specification does not provide sufficient direction and guidance as to the nature of antibodies that can induce cross-linking in vivo, broadly encompassed by the claimed invention.

While cross-linking antibodies in vivo may be accomplished by various antibody constructs, including multimeric antibodies, or whole antibodies that bind anti-PSGL antibodies that are not hamster antibodies,
the instant disclosure provides for insufficient guidance and direction towards the relevant, identifying characteristics of the "antibodies that bind to an anti-PSGL-1 antibody and induce apoptosis or cross-linking of a plurality of PSGL-1 antigens on the surface of T cell".

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. The specification does not describe nor enable any "antigen binding fragment of anti-PSGL-1 antibodies to induce apoptosis or to cross-linking of a plurality of PSGL-1 antigens on the surface of T cell" in the absence of administering the appropriate secondary cross-linking agent / antibody.

Without sufficient guidance, making and using any "antigen binding fragment of anti-PSGL-1 antibodies to induce apoptosis or to cross-linking of a plurality of PSGL-1 antigens on the surface of T cell" in the absence of administering the appropriate secondary cross-linking agent / antibody" in the claimed methods would have been unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

With respect to applicant's arguments, filed 02/01/2007, concerning the previous rejection under 35 USC 112, first paragraph, enablement;
the following is noted.

Applicant's amendment, filed 02/01/2007, have been fully considered but have not been found convincing as it applies to the New Grounds of Rejection with respect to administering any "antigen binding fragment of anti-PSGL-1 antibodies to induce apoptosis or to cross-linking of a plurality of PSGL-1 antigens on the surface of T cell" in the absence of administering the appropriate secondary cross-linking agent / antibody" in the claimed methods set forth herein.

Applicant argues in conjunction with the references submitted on the Supplemental IDS that the teachings of the present application and the state of the prior art, the skilled artisan could obtain a cross-linking antibody as recited in the claims without undue experimentation.

However, applicant has not provided sufficient direction and guidance in the specification as filed as how to make and to use such cross-linking antibodies in the claimed methods, as generically claimed
nor how to make and use antigen-binding fragments in the absence of cross-linking agents / antibodies, as broadly claimed.

Again as applicant acknowledge, applicant appears to be relying upon the disclosure of the anti-hamster Ig or rabbit anti-mouse Ig as a cross-linker antibody (e.g. see Example 3 on pages 19-20 and Example 10 on pages 26-27) to support an entire genus of "antibodies that bind to an anti-PSGL-1 antibody".

This invention encompasses any "antibody that binds to the monoclonal antibody and induces the cross-linking of a plurality of PSGL-1 antigens on the surface of cell" (e.g. see Summary of the Invention, particularly page 5, paragraph 3 of the instant specification),

yet the instant specification does not provide sufficient direction and guidance as to the nature of antibodies that can induce cross-linking in vivo, broadly encompassed by the claimed invention.

While cross-linking antibodies in vivo may be accomplished by various antibody constructs, including multimeric antibodies, or whole antibodies that bind anti-PSGL antibodies,

the instant disclosure provides for insufficient guidance and direction towards the relevant, identifying characteristics of the *"antibodies / antigen-binding fragments" that bind to an anti-PSGL-1 antibody and induce apoptosis or the cross-linking of a plurality of PSGL-1 antigens on the surface of T cell"* with respect to those antibodies or antigen-binding fragments lacking in the appropriate immunoglobulin Fc region.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth.

Without sufficient guidance, making and using any "antigen binding fragment of anti-PSGL-1 antibodies to induce apoptosis or to cross-linking of a plurality of PSGL-1 antigens on the surface of T cell" lacking in the appropriate immunoglobulin Fc region in the absence of administering the appropriate secondary cross-linking agent / antibody" in the claimed methods would have been unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

Applicant's arguments have not been found persuasive.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office Action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

19. For clarity and convenience and as pointed out previously,
for examination purposes, it appears that claimed methods which rely upon the elected species of administering an anti-PSGL-1 antibody and an "agent that binds to the monoclonal antibody and induces the cross-linking of plurality of PSGL-1 antigens on the surface of T cell appears free of the prior art.

Accordingly, the prior art rejections have been extended to read on the species of administering anti-PSGL-1 antibodies in the absence of administering a secondary "cross-linking agent".

Further, it has been noted by applicant that indicated that the claimed methods rely upon secondary cross-linking agents / antibodies to accomplish the claimed mode of action (i.e., apoptosis), *whether or not the anti-PSGL-1 antibodies are administered even in the absence of cross-linking agents/antibodies* (e.g., see page 13, lines 4-9 of Applicant's Remarks, filed 02/01/2007).

As indicated in the prior art rejections of record, it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosures of administering anti-PSGL-1 antibodies to inhibit P-selectin- / PSGL-1-mediated interactions, including immune responses such as the elected autoimmune disease diabetes.

However, certain prior art disclosures are silent on the claimed recitation of "apoptosis-inducing anti-PSGL-1 antibody or antigen-binding fragment thereof" "wherein the binding of the antibody or antigen-binding fragment thereof to PSGL-1 on the surface of the T cell or NK cell induces apoptosis of the T cell or NK cell".

As pointed out above, the Office is not equipped to conduct comparisons. Applicant has been invited to provide clarity and objective evidence as to the mechanism of action by which the administration of anti-PSGL-1 antibodies can reduce T cell mediated immune responses, including autoimmunity such as diabetes in the absence of a secondary cross-linking agent.

Also, as noted herein and of record, co-inventors own publication Chen et al. (Blood 104: 3233-3242, 2004) indicates that PSGL-1 mediated death via PSGL-1-specific antibodies is stage dependent in that it affects mature activated T cells (see entire document, particularly the Discussion).

Therefore, applicant's reliance on "inducing a signal transduction that results in the death of the T cell thereby reducing a T cell-mediated immune response in the individual" appears based not entirely on the nature of the anti-PSGL-1 antibody but rather based on the presence of PSGL-1 expressing mature activated T cells.

11. Claims 1, 3, 6, 10-12, 17, 19, 22-24 and 38 are rejected under 35 U.S.C. § 102(b) as being anticipated by Larsen et al. (U.S. Patent No. 5,840,679) (see entire document) essentially for the reasons of record and in further evidence of Chen et al. (Blood 104: 3233-3242, 2004).

Applicant's arguments, filed 02/01/2007, in conjunction with the Lin 132 Declaration, have been fully considered but are not found convincing essentially for the reasons of record.

Applicant submits in conjunction with the Lin Declaration that not all anti-PSGL-1 antibodies can induce T cell apoptosis.

Applicant relies upon the assertion that applicant has discovered a new epitope specificity if apoptosis-inducing anti-PSGL-1 antibodies.

However, it is noted that the claims do not recite a particular antibody epitope per se.

Also, it is noted that applicant in conjunction with Lin have indicated that the claimed methods and modes of action rely upon secondary cross-linking agents/antibodies and/or in the absence of secondary cross-linking agents/antibodies.

Applicant in conjunction with the Lin 132 Declaration disagrees with that the position of the examiner that the evidentiary reference Chen indicates that it is the presence of PSGL-1 on mature activated T cells (e.g., cell stage dependent) that governs the claimed mode of action rather than the nature (e.g. apoptosis-inducing anti-PSGL-1 antibody).

Applicant relies upon the current amendment to recite "apoptosis inducing anti-PSGL-1 antibody) and "the binding of the antibody or antigen-binding fragment thereof to PSGL-1 on the surface of the T cell or NK cell induces apoptosis of the T cell or NK cell to obviate this rejection.

Applicant in conjunction with the Lin 132 Declaration note that certain anti-PSGL-1 antibodies, but not all anti-PSGL-1 antibodies, are capable inducing apoptosis or mature, activated T cells and that certain apoptosis-inducing anti-PSGL-1 antibodies do not interfere with PSGL-1-mediated interactions with other selectins.

More pointedly, applicant asserts in conjunction with the Lin 132 Declaration that neutralizing and non-neutralizing antibodies taught by the prior art Larsen et al. would not necessarily and inevitably involve anti-PSGL-1 antibodies that are capable of inducing apoptosis of T cells.

Applicant further submits that Larsen et al. is silent about apoptosis as well as the cross-linking of anti-PSGL-1 antibodies by any means.

However, applicant in conjunction with the Lin Declaration have indicated that the claimed methods and modes of action rely upon secondary cross-linking agents/antibodies and/or in the absence of secondary cross-linking agents/antibodies (e.g., via Fc receptors).

With respect to the evidentiary reference of Chen et al. concerning the cell stage dependence of the claimed methods,
applicant submits that Chen et al. is not mutually exclusive in its teaching.

Rather, much of applicant's arguments in conjunction with the Lin Declaration appear to rely upon an asserted new mechanism of action of anti-PSGL-1 antibodies rather than focusing on new anti-PSGL-1 antibody epitopes or other characteristics.
Also, the anti-PSGL-1 antibodies are claimed in terms of function (e.g., apoptosis-inducing).

Again, the mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Even though applicant has proposed or claimed the mechanism by which anti-PSGL-1 antibodies may reduce T cell mediated immune responses does not appear to distinguish the prior art teaching the same or nearly the same methods to achieve the same end result.

Further, it is noted in the in teachings of Larsen et al. concerning PSGL-1-specific inhibitory antibodies, such PSGL-1-specific neutralizing antibodies bind to PSGL-1, or to complex carbohydrate moieties characteristic of PSGL-1 (e.g., see column 18, paragraph 2) as well as inhibitory antibodies that bind particularly fragments of PSGL-1, including peptides having a sulfated tyrosine (e.g., see column 18, paragraph 4) and exemplified anti-PSGL-1 antibodies that demonstrated complete inhibition of PSGL-1 : P-selectin binding (e.g., see Example 7 on columns 29-30) as well as providing appropriate screening assays (e.g., see columns 19-20; Example 7 on columns 29-30).

Given these specificities and properties of neutralizing anti-PSGL-1 antibodies to be employed in therapeutic methods to treat diabetes

and the lack of a requirement for additional cross-linking antibodies / agents to be administered in combination;

it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure.

See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001).

"{i}t is a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable". In re Woodruff, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990). The mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

The following of record is reiterated, in part, for applicant's convenience.

It is still difficult to ascertain the distinctions between the claimed and prior art methods, which inhibit T cell-mediated immune responses with PSGL-1-specific antibodies.

Therefore, applicant's reliance on "inducing apoptosis of T cells and NK cells which reduce cell-mediated immune response in the individual" appears based not on the nature of the anti-PSGL-1 antibody but rather based, in part, on the presence of PSGL-1 expressing mature activated T cells.

Applicant has previously argued that the prior art is drawn to the use of antagonistic anti-PSGL-1 antibodies, while the instant claims are drawn to the use of agonistic antibodies.

Again, neither the claims nor the specification make it clear that the instant antibodies are necessarily agonistic antibodies and agonistic in terms of what endpoints, while the prior art taught antagonistic antibodies.

As noted by co-inventors own publication Chen et al. (Blood 104: 3233-3242, 2004), the issue appears not to be one of agonistic or antagonistic antibodies but rather the presence of PSGL-1 expressing mature activated T cells during the administration of PSGL-1-specific antibodies.

It is unclear how applicant is making this distinction, given that the claims rely upon anti-PSGL antibodies with no mention of agonistic properties and both the instant and prior art anti-PSLG-1 antibodies are administered to inhibit T cell mediated immune responses.

The reduction of T cell mediated immune responses may occur via multiple modes of action.

Again, while applicant relies upon in vitro analysis and cross-linking of anti-PSGL antibodies under in vitro experimental conditions to show evidence of apoptosis, applicant does not provide sufficient objective evidence that the administration of anti-PSGL antibodies in vivo does or does not require cross-linking to achieve the decrease in T cell numbers and T cell mediated immune responses in view of antibody treatment of an experimental autoimmune diabetes model (see instant Example 11).

While the invention may be based on the discovery that T cells can be depleted and/or induced to undergo apoptosis by the engagement of the T cell surface antigen PSGL (e.g. Summary of the Invention and applicant's arguments),
there is insufficient objective evidence that the treatment of anti-PSGL-1 antibodies in the prior art do not result in the claimed cell death of T cells via cross-linking (e.g. via Fc- FcR binding) and/or the presence of PSGL-1 expressing mature activated T cells during the administration of PSGL-1-specific antibodies.

Also, while Example 11 discloses the use of anti-PSGL-1 antibodies to treat an experimental model of diabetes, there is insufficient objective evidence that the reduction of T cell mediated immune response is accomplished via the death of the T cells and does not rely upon other mechanisms in vivo.

Although the reference is silent about the induction of T cell or NK cell death or apoptosis as well as identifying the T cell as activated, $CD3^+$, $CD4^+$, or $CD8^+$ as well as the depletion of T cells, it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure.

The products employed in the instant methods and the prior art are defined in terms of anti-PSGL-1 antibodies. Comparison of the instant products with prior art is difficult since the Office is not equipped to manufacture the claimed product and/or prior art products that appear to be related and conduct comparisons

Applicant is invited to clarify the distinctions between the properties of anti-PSGL-1 antibodies and the instant anti-PSGL-1 antibodies and claimed the antibodies accordingly.

As noted above, it is still unclear the applicability of prior art,
given the breadth of the instant claims and that multiple mechanisms and characteristics may be involved in reducing cell-mediated immune responses with PSGL-1-specific antibodies;
it is still difficult for the examiner to determine
whether applicant has discovered a new mode of action (e.g. induction of apoptosis) of anti-PSGL-1 antibodies,
whether applicant has discovered a new epitope specificity of apoptosis-inducing anti-PSGL-1 antibodies,
whether applicant is relying upon secondary cross-linking agents / antibodies to accomplish this newly discovered mode of action and/or
whether the administration of anti-PSGL-1 antibodies even in applicant's model operate via apoptosis in vivo in the absence of secondary cross-linking agents / antibodies.

As indicated herein, applicant's reliance on "inducing apoptosis of T cells and NK cells thereby reducing a T cell-mediated immune response in the individual" appears based on the nature of the anti-PSGL-1 antibody, the nature of the specificity of the anti-PSGL-1 antibody as well as the presence of PSGL-1 expressing mature activated T cells during the administration of PSGL-1-specific antibodies.

Therefore the prior art stands at this time, given it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure.

See the previous Office Action for a more complete analysis of the prior art rejection.

12. New Grounds of Rejection.

Although Lazarovits et al. (US 2004/0002450 A1) does not teach treating the elected species of diabetes per se, Lazarovits et al. does teach treating autoimmune diseases with PSGL-1-specific antibodies that appear to be consistent with applicant's arguments and interpretation of "apoptosis-inducing PSGL-1 antibodies".

Claims 1, 3, 4, 6, 10-13, 17, 19, 20, 22-25 and 38 are rejected under 35 U.S.C. § 102(e) as being anticipated by Lazarovits et al. (US 2004/0002450 A1) (see entire document)
and as further evidenced by the Lin 132 Declaration, filed 02/01/2007.

Lazarovits et al. teach methods of treating inflammation, including autoimmune diseases with PSGL-1-specific antibodies (e.g., see paragraphs [00555] – [0057]; Summary of the Invention on paragraphs [0059] – [0144]; Detailed Description of the Invention) , including the Y1, Y17 and KPL1 epitopic specificities (e.g., see Selectins and PSGL-1 on paragraphs [0029] – [0042] ; Summary of the Invention; Detailed Description of the Invention; and Examples), including antibody constructs (e.g., see paragraphs [0474] – [0523]) as well as their use to monitor disease states (e.g., see paragraph 0523]).

The Lin 132 Declaration, filed 02/01/2007, acknowledges that KPL1-specific PSGL-1-specific antibodies can induce apoptosis (e.g., see Exhibit C).

Also, it is noted that applicant in conjunction with Lin have indicated that the claimed methods and modes of action rely upon secondary cross-linking agents/antibodies and/or in the absence of secondary cross-linking agents/antibodies.

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced PSGL-1-specific antibodies in methods to treat certain inflammatory diseases, including autoimmune diseases.

Given these specificities and properties of neutralizing anti-PSGL-1 antibodies to be employed in therapeutic methods to treat diabetes
and the lack of a requirement for additional cross-linking antibodies / agents to be administered in combination;
it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure.
See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001).

"{i}t is a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable". In re Woodruff, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990). The mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

13. Claims 1, 3, 4, 6, 10-13, 17, 19, 20, 22-25 and 38 are rejected under 35 U.S.C. § 103(a) as being unpatentable over by Larsen et al. (U.S. Patent No. 5,840,679) in view of Trembleau et al. (J. Immunol. 163 : 2960 – 2968, 1999), Yago et al. (J. Immunol. 161 : 1140 –1145 (1998), Hirata et al. (J. Exp. Med. 192: 1669 – 1675, 2000) and Cobbold et al. (U.S. Patent No. 6,056,956)
and as futher evidenced by Chen et al. (Blood 104: 3233-3242, 2004) essentially for the reasons of record.

Applicant's arguments, filed 02/02/2007, and the examiner's rebuttal are essentially the same set forth above.

Therefore, applicant's arguments have been fully considered but are not found convincing essentially for the reasons of record.

See the previous Office Action and the Section above for a more complete analysis of the prior art rejection.

While the invention may be based on the discovery that T cells can be depleted and/or induced to undergo apoptosis by the engagement of the T cell surface antigen PSGL (e.g. Summary of the Invention and applicant's arguments),
there is insufficient objective evidence that the treatment of anti-PSGL-1 antibodies in the prior art do not result in the claimed cell death of T cells via cross-linking (e.g. via Fc- FcR binding) and/or the presence of PSGL-1 expressing mature activated T cells during the administration of PSGL-1-specific antibodies.

Also, it is noted that applicant in conjunction with Lin have indicated that the claimed methods and modes of action rely upon secondary cross-linking agents/antibodies and/or in the absence of secondary cross-linking agents/antibodies.

Further, it is noted the reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant. See MPEP 2144.

Applicant's arguments have not been found persuasive.

14. New Grounds of Rejection.

Claims 1, 3, 4, 6, 10-13, 17, 19, 20, 22-25 and 38 are rejected under 35 U.S.C. § 103(a) as being unpatentable over by Larsen et al. (U.S. Patent No. 5,840,679) in view of Trembleau et al. (J. Immunol. 163: 2960 – 2968, 1999), Yago et al. (J. Immunol. 161 : 1140 –1145 (1998), Hirata et al. (J. Exp. Med. 192: 1669 – 1675, 2000) and Cobbold et al. (U.S. Patent No. 6,056,956)
and as futher evidenced by Chen et al. (Blood 104: 3233-3242, 2004) essentially for the reasons of record.
and further in view of Snapp et al. (Blood 91: 154-164, 1998) (1449; #AS) AND/OR Lazarovits et al. (US 2004/0002450 A1) (see entire document)
and as further evidenced by the Lin 132 Declaration, filed 02/01/2007.

The prior art of record does not teach the particular KPL1-specificity in inhibitory anti-PSGL-1 antibodies.

As indicated above and as evidenced by the 132 Lin Declaration, filed 02/01/2007, the Lin 132 Declaration, filed 02/01/2007, acknowledges that KPL1-specific PSGL-1-specific antibodies can induce apoptosis (e.g., see Exhibit C).

Snapp et al. and Lazarovits et al. have been added for their teachings of alternative anti-PSGL-1 antibodies to substitute in the methods taught by Larsen et al., wherein the anti-PSGL-1 antibody specificities taught by Snapp et al. and Lazarovits et al. have the property of PSGL-1 apoptosis-inducing antibodies asserted by applicant and as evidenced by the Lin 132 Declaration, filed 02/02/2007.

Snapp et al. teach the KPL1 anti-PSGL-1 antibody specificity, wherein KPL1 completely inhbiting P-selectin-mediated interactions, including interactions with lymphoid cells such as T cells and NK cells (see entire document, including Abstract, Results and Discussion).

Lazarovits et al. teach methods of treating inflammation, including autoimmune diseases with PSGL-1-specific antibodies (e.g., see paragraphs [00555] – [0057]; Summary of the Invention on paragraphs [0059] – [0144]; Detailed Description of the Invention), including the Y1, Y17 and KPL1 epitopic specificities (e.g., see Selectins and PSGL-1 on paragraphs [0029] – [0042] ; Summary of the Invention; Detailed Description of the Invention; and Examples), including antibody constructs (e.g., see paragraphs [0474] – [0523]) as well as their use to monitor disease states (e.g., see paragraph 0523]).

One of ordinary skill in the art at the time the invention was made would have been motivated to substitute the anti-PSGL-1 antibodies with the Y1, Y17 and KPL1 epitopic specificities in inhibiting inflammatory or autoimmune conditions targeted by PSGL-1 antagonists, given their highly inhibitory effects on PSGL-1-mediated interactions, including their antagonistic effects on lymphoid cells such as T cells and NK cells, as taught by Snapp et al. and Lazarovits. A person of ordinary skill in the art at the time the invention was made would have been motivated by taking the advantages of the specificities and properties of the highly inhibitory properties of the Y1, Y17 and KPL1 PSGL-1 epitopic specificities to modify the prior art teachings to treat inflammatory or autoimmune conditions with an expectation of success, since such properties and advantages are consistent with human therapeutic regimens associated with treating said conditions at the time the invention was made. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

15. Claims 1, 3, 4, 6, 10-13, 17, 19, 20, 22-25 and 38 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 4, 8, 9, 12-15, 19-22, 23, 26, 30, 31, 34-38 of copending application USSN 10/662,906. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are drawn to the same or nearly the same methods of preventing or reducing T cell-mediated immune responses with the same nearly the same PSGL-1-specific antibodies. Therefore, the copending claims either anticipate or render obvious one another.

It is noted that the copending claims recite a "multimeric compound that binds at least two PSGL-1 proteins". Given that the copending claims also recite "anti-PSGL-1 antibodies" and that antibodies have two binding sites, the copending claims appear to read on the instant claims drawn to the essentially the same methods relying upon PSGL-1 antibodies.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 3, 4, 6, 10-13, 17, 19, 20, 22, 23, 24 and 25 are directed to an invention not patentably distinct from claims 1, 4, 8, 9, 12-15, 19-22, 23, 26, 30, 31, 34-38 of commonly assigned USSN 10/662,906 for the reasons set forth above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned USSN 10/662,906, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

Applicant's amendment, filed 02/01/2007 acknowledged the obvious double patenting rejection, but requests it to be held in abeyance until such time as the present or copending application issues into a patent.

16. No claim allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-272-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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